

USP16 controls stem cell number: implications for Down Syndrome

Grant Award Details

USP16 controls stem cell number: implications for Down Syndrome

Grant Type: Basic Biology III

Grant Number: RB3-05066

Project Objective: Project objective is to understand the role of USP16 in regulating normal and Down's Syndrome stem cells as well as the activity of this component in suppressing tumor formation.

Investigator:

Name:	Michael Clarke
Institution:	Stanford University
Type:	PI

Disease Focus: Genetic Disorder

Human Stem Cell Use: Adult Stem Cell

Award Value: \$1,263,826

Status: Closed

Progress Reports

Reporting Period: Year 1

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Reporting Period: Year 3

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Grant Application Details

Application Title: USP16 controls stem cell number: implications for Down Syndrome

Public Abstract: Stem cells are endowed with the ability to self-renew, that means to give rise to other cells with the same potential to regenerate a tissue. Recently, we found a gene that also regulates this mechanism. In addition, expression of high levels of this gene can reduce the number of stem cells in the bone marrow and possibly the brain. This gene is expressed in the Chromosome 21 and hence can potentially contribute to the pathology of people with Down Syndrome (people with Down Syndrome has three copies of Chromosome 21). In line with that, we observed that mouse models for Down Syndrome have less stem cells in their bone marrow. We therefore want to study the mechanism of action of this gene and its effects on stem cells in the bone marrow and other tissues.

Outcomes from this study will shed more light in understanding not only the normal process of stem cell maintenance, but also in deciphering the complex biology underlying Down Syndrome. In particular, this study will potentially help to understand why Down Syndrome carriers have a defect in learning. We hypothesize that a defect in neural stem cells leads to abnormal brain development. If so, then pharmacologic agents that inhibit the function of this gene might ameliorate the pathology of Down Syndrome.

Another important aspect of our research on this pertains to cancer development: indeed cancer initiating cells take advantage of the normal self-renewal machinery to proliferate without restraint. Our preliminary data suggest that high levels of this gene could potentially counteract some solid tissue tumors, putting a brake on cancer cells proliferation. Interestingly, people with Down Syndrome have a much lower risk of developing solid tumors than the general population. We will use human cancer samples, in particular breast and colon tumors, that we receive directly from Stanford Hospital to analyze this gene's contribution to cancer development. These studies will give us important hints to discover alternative strategies for cancer treatment.

Statement of Benefit to California: The goal of the proposed research is to shed more light in understanding not only the normal process of stem cell maintenance, but also in deciphering the complex biology underlying the Down Syndrome. This study will potentially help to understand i) whether a defect in stem cell self renewal contributes to the Down Syndrome phenotype, ii). why Down Syndrome patients have a lower risk of solid tumors. These studies potentially could identify an enzyme which could be drugged to partially ameliorate Down Syndrome pathology. This clearly would provide great benefits to the people of California by minimizing suffering of patients and families while also decreasing the costs associated with care of these patients.

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